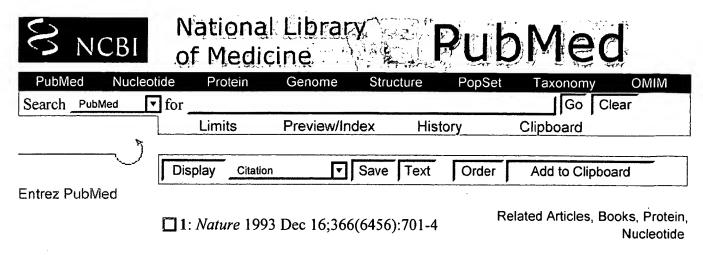


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p21 is a universal inhibitor of cyclin kinases.

Xiong Y, Hannon GJ, Zhang H, Casso D, Kobayashi R, Beach D

Howard Hughes Medical Institute, Cold Spring Harbor Laboratory, New York 11724.

Related Resources

Deregulation of cell proliferation is a hallmark of neoplastic transformation. Alteration in growth control pathways must translate into changes in the cell-cycle regulatory machinery, but the mechanism by which this occurs is largely unknown. Compared with normal human fibroblasts, cells transformed with a variety of viral oncoproteins show striking changes in the subunit composition of the cyclin-dependent kinases (CDKs). In normal cells, CDKs exist predominantly in multiple quaternary complexes, each containing a CDK, cyclin, proliferating cell nuclear antigen and the p21 protein. However, in many transformed cells, proliferating cell nuclear antigen and p21 are lost from these multiprotein enzymes. Here we have investigated the significance of this phenomenon by molecular cloning of p21 and in vitro reconstitution of the quaternary cell-cycle kinase complexes. We find that p21 inhibits the activity of each member of the cyclin/CDK family. Furthermore, overexpression of p21 inhibits the proliferation of mammalian cells. Our results indicate that p21 may be a universal inhibitor of cyclin kinases.

Comment in:

Nature. 1993 Dec 16;366(6456):634

MeSH Terms:

- Amino Acid Sequence
- Animal
- Base Sequence
- Cell Cycle*
- Cell Division
- Cell Line
- Cloning, Molecular
- Cyclins/metabolism*

- Cyclins/isolation & purification
- Cyclins/genetics
- DNA
- Mice
- Molecular Sequence Data
- Moths
- Protein Kinases/antagonists & inhibitors*
- Protein p53/metabolism
- RNA, Messenger/analysis
- Recombinant Proteins/metabolism
- Recombinant Proteins/isolation & purification
- Recombinant Proteins/genetics
- o Support, Non-U.S. Gov't
- Support, U.S. Gov't, P.H.S.

Substances:

- Protein Kinases
- o p34PSK-J3 kinase
- DNA
- Recombinant Proteins
- RNA, Messenger
- Protein p53
- Cyclins
- Cip1 protein

PMID: 8259214



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Department of Health & Human Services
Freedom of Information Act | Disclaimer

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     R; Xiong, Y.; Hannon, G.J.; Zhang, H.; Casso, D.; Kobayashi, R.; Beach, D.
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     Cell 75, 805-816, 1993
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Hum. Mol. Genet. 4, 1089-1092, 1995
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15-DEC-1998 (Rel. 37, Last annotation update)
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     -!- SIMILARITY: THE N-TERMINAL OF CIP1 AND KIP ARE SIMILAR.
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         (ANTILEUKEMIC COMPOUND) AND BY IFN-BETA.
CC
     -!- SIMILARITY: THE N-TERMINAL OF CIP1 AND KIP ARE SIMILAR.
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     This SWISS-PROT entry is copyright. It is produced through a collaboration
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171 KRRLIFSK 178

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     TITLE OF INVENTION: SENESCENT CELL DERIVED INHIBITORS OF
     TITLE OF INVENTION: DNA SYNTHESIS
     NUMBER OF SEQUENCES: 2
     CORRESPONDENCE ADDRESS:
       ADDRESSEE: HOWREY & SIMON
       STREET: 1299 PENNSYLVANIA AVE., N.W.
       CITY: WASHINGTON STATE: D.C.
       COUNTRY: USA
       ZIP: 20004
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     PRIOR APPLICATION DATA:
       APPLICATION NUMBER: US 07/808,523
       FILING DATE: 16-DEC-1991
     ATTORNEY/AGENT INFORMATION:
       NAME: AUERBACH, JEFFREY I.
       REGISTRATION NUMBER: 32,680
       REFERENCE/DOCKET NUMBER: 225-102-CIP
     TELECOMMUNICATION INFORMATION:
       TELEPHONE: (202) 383-7451
       TELEFAX: (202) 383-6610
   INFORMATION FOR SEQ ID NO: 2:
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       ORGANISM: HOMO SAPIENS
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     TITLE OF INVENTION: Cyclin Complex Rearrangement and Uses
     TITLE OF INVENTION: Related Thereto NUMBER OF SEQUENCES: 6
     CORRESPONDENCE ADDRESS:
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ADDRESSEE: LAHIVE & COCKFIELD
       STREET: 60 State Street
;
       CITY: Boston
       STATE: MA
       COUNTRY: USA
       ZIP: 02109
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       FILING DATE: 19-NOV-1993
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       APPLICATION NUMBER: US 07/991,997
       FILING DATE: 17-DEC-1993
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       APPLICATION NUMBER: US 07/963,308
       FILING DATE: 16-OCT-1993
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       APPLICATION NUMBER: US 07/888,178
       FILING DATE: 26-MAY-1993
     PRIOR APPLICATION DATA:
       APPLICATION NUMBER: US 07/701,514
     FILING DATE: 16-MAY-1993 ATTORNEY/AGENT INFORMATION:
       NAME: Vincent, Matthew P.
       REGISTRATION NUMBER: 36,709
       REFERENCE/DOCKET NUMBER: MII-026
     TELECOMMUNICATION INFORMATION:
       TELEPHONE: (617) 227-7400
       TELEFAX: (617) 227-5941
   INFORMATION FOR SEQ ID NO: 6:
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; Patent No. 5688665
; GENERAL INFORMATION:
     APPLICANT: Massague, Joan
     APPLICANT: Roberts, James M.
APPLICANT: Koff, Andrew
APPLICANT: Polyak, Kornelia
     TITLE OF INVENTION: Isolated p27 Protein, Nucleic Acid Molecules NUMBER OF SEQUENCES: 19
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     CORRESPONDENCE ADDRESS:
       ADDRESSEE: LAHIVE & COCKFIELD
       STREET: 60 State Street, suite 510
       CITY: Boston
       STATE: Massachusetts
       COUNTRY: USA
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       REGISTRATION NUMBER: 36,709
       REFERENCE/DOCKET NUMBER: MII-079CP
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       TELEPHONE: (617)227-7400
       TELEFAX: (617)227-5941
   INFORMATION FOR SEQ ID NO: 4:
     SEQUENCE CHARACTERISTICS:
      LENGTH: 164 amino acids
       TYPE: amino acid
       TOPOLOGY: linear
     MOLECULE TYPE: peptide FRAGMENT TYPE: internal
US-08-275-983B-4
  Query Match 100.0%; Score 38; DB 1; Length 164; Best Local Similarity 100.0%; Pred. No. 0.25;
           8; Conservative 0; Mismatches
                                                    0; Indels
                                                                  0; Gaps
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        1 KRRLIFSK 8
Qу
          11111111
Db
      154 KRRLIFSK 161
RESULT 5
US-08-574-043A-2
; Sequence 2, Application US/08574043A
; Patent No. 5807692
; GENERAL INFORMATION:
     APPLICANT: Kinzler, Kenneth W. APPLICANT: El-Deiry, Wafik
     APPLICANT: Vogelstein, Bert
     TITLE OF INVENTION: p21WAF1 Derivatives and Diagnostic TITLE OF INVENTION: Methods
     NUMBER OF SEQUENCES: 7
     CORRESPONDENCE ADDRESS:
       ADDRESSEE: Banner & Allegretti, LTD
       STREET: 1001 G Street, NW suite 1100
       CITY: Washington
STATE: DC
       COUNTRY: USA
       ZIP: 20001
     COMPUTER READABLE FORM:
       MEDIUM TYPE: Floppy disk
       COMPUTER: IBM PC compatible
       OPERATING SYSTEM: PC-DOS/MS-DOS
       SOFTWARE: PatentIn Release #1.0, Version #1.25
     CURRENT APPLICATION DATA:
       APPLICATION NUMBER: US/08/574,043A
       FILING DATE:
       CLASSIFICATION: 514
     ATTORNEY/AGENT INFORMATION:
       NAME: Kagan, Sarah A.
       REGISTRATION NUMBER: 32,141
       REFERENCE/DOCKET NUMBER: 01107.49698
     TELECOMMUNICATION INFORMATION:
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